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MEDICAL RESEARCH IN MALARIA*

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The following is a brief outline of the work done during the past year by members of the Department of Medical Zoology, School of Hygiene and Public Health, Johns Hopkins University.

(I) Efforts have been made to discover a therapeutic agent equal to or better than quinin. This work has been in progress since July 1, 1923, under the direction of Dr. Hegner, with Dr. G. H. Boyd in charge from July 1, 1923 to June 30, 1924, and Mr. Ernest Hartman in charge since July 1, 1924. Synthetic quinin derivatives have been obtained from Dr. Jacobs of the Rockefeller Institute and these have been experimentally used on canaries suffering from bird malaria. The result desired is to find an agent that will bring about the destruction of all of the parasites in the body of the host and hence prevent relapse.

(II) The relation of malarial organisms to mosquitoes in nature has been studied. Dr. F. M. Root spent the summer of 1923 at Leesburg, Georgia, dissecting mosquitoes in order to determine which species actually transmit malaria. His results are not yet available.

(III) Complement fixation tests have been attempted for malaria carriers. The work was begun by Drs. H. C. Clark and R. W. Hegner at Tela, Honduras, during the summer of 1924 and will probably be continued during the coming school year.

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*Report from Member of Sub-Committee on Medical Research, National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Eighteenth Annual Meeting, New Orleans, La., Nov. 24-27, 1924.

PROBLEMS FOR FURTHER STUDY

(I) Studies should be made of the life-cycle of malaria parasites in the vertebrate host. Questions of importance are:

(1) Where are the parasites located in the body at various stages in the course of the infection and in what stages in their life-cycles? The distribution of the stages is known to differ in falciparum from that of the other two species. Why do specimens of falciparum clog up the capillaries? What factors bring about these differences in distribution, etc., and what are their relations to virulence, latency, relapse, etc.?

(2) Is the malarial parasite inside or outside of the red cell? In all stages? Do the parasites migrate from one cell to another?

(3) Is there a filterable stage in the life-cycle, especially during the period between relapses when no parasites can be found in the peripheral blood?

(4) When and where, does the change take place from schizonts to gametocytes? Factors? Does the sex of the host have any influence on the production and sex of the gametocytes?

(5) If the falciparum disappears and vivax takes its place as is claimed by some, what are the stages in this change and how is it brought about?

(II) Studies are likewise needed of the life-cycle of malaria parasites in mosquitoes.

(1) In nature, what is the influence of temperature moisture, latitude and altitude on sporogony in the mosquito? Length of different stages? Numbers of oocysts? Numbers and distribution of sporozoites?

(2) Effects of starvation, diet, etc., on stages in life-cycle in mosquitoes? Duration of stages? Numbers? Length of infectivity?

(3) Are stages in sporogony as worked out by Grassi correct?

(4) Does the environment of the mosquito or its larva or pupa have any effect on its infectivity? Humidity, temperature, salinity of water, altitude?

(5) Are different species of mosquitoes responsible for the appearance of vivax early and falciparum later in the season?

(6) Are mosquitoes responsible for the local appear-

ance of malaria? Plasmodium malariae may be abundant in a spot surrounded by vivax and falciparum but free from malariae.

(7) Do mosquitoes suffer from infection? Do non-infected mosquitoes live longer than infected mosquitoes?

(8) Effects of hibernation and estivation on sporogony? Do oocysts degenerate?

(9) How many gametocytes are necessary to infect mosquitoes?

(10) How many oocysts are necessary to produce an infective mosquito?

(11) Are mosquitoes susceptible to mixed infections? Can they transmit them to man? If they can, does this prove plurality of species?

(12) There exist relatively impossible mosquito hosts. Why is there not infection in all hospitable hosts?

(III) Problems of relapse in malaria are concerned with:

(1) Parthenogenesis. What is the status of this phenomenon?

(2) Do old red cells become immune? Are young cells more frequently parasitized? Would relapse result from rapid increase of young cells?

(3) Is relapse due to changes in blood plasma which make it easier for merozoites to parasitize cells, or to changes in the inhibiting power of leuocytes?

(4) Can relapse be brought on after administering quinin?

(5) What is responsible for latency, i.e., the period between inoculation and symptoms?

(6) The changes in the body that are responsible for relapses may be determined by determining the constant factor of altitude, cold, etc., and provocatives.

(7) Is there a resistant stage or unknown stage of parasite that brings on relapses?

(IV) The species problem is in many ways unsettled.

(1) Is there a *tenue* stage in the life-cycle of falciparum?

(2) Are the species in man and primates the same?

(3) How many human species are there?

(4) Are there two species or subspecies of falciparum?

(5) If a mosquito is fed on mixed infection will it transmit a mixed infection?

(6) Is virulence related to different races of parasites?

(V) What is the relation of parasite to the resistance of host and blood reactions?

(1) Is immunity acquired?

(2) Is complement fixation in malaria with antigens prepared from the cultures or organs?

(3) What is the relation between the number of parasites in the blood and clinical symptoms?

(4) What brings about clinical symptoms?

(5) Does dengue give immunity?

(6) What is responsible for the pathogenicity of falciparum?

(7) Do provocatives increase asexual reproduction or force parasites out into the blood?

(VI) What are the effects of quinin on parasites?

(1) Effects on various stages of different parasites in blood?

(2) Quinin prophylaxis under controlled conditions.

(3) Effects on parasites in non-quininized cases after various types of doses.

(4) Effects on mosquitoes of ingesting blood containing parasites as well as quinin.

(VII) Identification of carriers might be possible through study of:

(1) Spleens.

(2) Complement fixative.

(3) Leucocyte method.

(4) Thick and thin films.

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